phenotypic abnormalities. The most characteristic features are microcephaly, a thin downturned mouth, prominent nose, micrognathia, small deep set eyes, short neck, simian crease, anomalies of the hands and feet, with generally normal ears and genitalia. Also commonly present are a low birthweight at term and the later development of epilepsy with an abnormal electroencephalogram. All these features were present in our patient, who appears to be the oldest recorded case. An adolescent girl was reported by Muldal et al[10] and she did have early puberty.

The chromosome complement seen in this patient arose at maternal oogenesis by 3:1 disjunction at the first meiotic division, the segregation resulting in the normal chromosomes 3 and 14 and the 14q– fragment moving to the same pole at anaphase I. At fertilisation, the father's normal chromosomes 3 and 14 made his complement 47,XY,+14q–. The error leading to this chromosome complement could not have arisen in any other way. However, we do not know if the translocation arose in the mother de novo, or was inherited from her father (who was dead). It would seem likely that the translocation arose de novo in the mother as none of her sibs carried it, which would be unusual if the father was a carrier. Other families reported in which an unbalanced proband had arisen by 3:1 disjunction from a carrier mother showed many carriers in the sibships of both the proband and the carrier mother. For example, Simpson and Zellweger[2] found five carriers and only one normal sib of the mother of their proband, whose sib was also a carrier, and in their case the translocation was also onto chromosome 3. In our family, the abnormality will have 'died out' after one generation.

In their very extensive study of unbalanced offspring derived from 3:1 meiotic disjunction in reciprocal translocation carriers, Lindenbaum and Bobrow[11] showed that there were certain characteristic features in these cases. There was no evidence of infertility among the carriers, there was a high incidence of spontaneous abortions (38% overall), which was higher in these 3:1 cases than in the offspring of reciprocal translocation carriers in general, there was no advanced maternal age effect, and frequent involvement of the acrocentric chromosomes was noted. The family described here shows all these features, except that a maternal age effect was evident.

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Partial trisomy of the short arm of chromosome 8 resulting from balanced maternal translocation

SUMMARY Extra chromosomal material on the long arm of chromosome 15 was found in an infant with growth retardation, dysmorphic features, skeletal abnormalities, and congenital heart defect. The phenotypically normal mother had a balanced translocation between the short

arm of chromosome 8 and the long arm of chromosome 15: 46,XX,t(8;15)(p12;q25). Thus, the patient was partially trisomic for the short arm of chromosome 8 (p12→pter).

Comparison of the clinical data obtained from patients with partial trisomy of the short arm of chromosome 8 with those of full trisomy 8 (Warkany's syndrome) suggests that most of the clinical features of Warkany's syndrome require excess material from both the short and long arm of chromosome 8.

Partial trisomy of the short arm of chromosome 8 has been reported in a few patients with diverse clinical and cytogenetic features[1][2] and has been reviewed by Lazjuk *et al*.[3] The purpose of this communication is to describe another case of partial trisomy of 8p with more severe clinical features than those of well defined trisomy 8 (Warkany's) syndrome. The validity of the proposed clinical mapping of chromosome 8 was tested with trisomy 8 and 8p trisomy.

Case report

The patient (III.1, fig 1), a 3-month-old white male, was a 2580 g, term infant born to a 25-year-old healthy primigravida. The pregnancy, labour, and delivery were uneventful. There was no exposure to known teratogenic agents and alcohol intake during the pregnancy was denied. The patient's neonatal course was uneventful; however, he was a poor feeder. Because of the poor weight gain and perioral cyanosis, he was admitted to St Louis Children's Hospital. The 31-year-old father was healthy and parental consanguinity was denied. The family history was unremarkable except for a history of multiple miscarriages in the maternal grandmother.

The proband's development was delayed. He began following objects at 2 months and he was not able to smile or hold his head up at 3 months.

Physical examination at 3 months revealed an underdeveloped infant with dysmorphic features. His weight (2880 g), height (50·5 cm), and head circumference (36 cm) were all below the 5th centile for his age. There was mild facial asymmetry and a skin haemangioma on the mid-forehead (fig 2). The eyes were almond-shaped with mild anti-mongoloid slanting. The inner canthal distance was 2·5 cm (between 75th and 97th centile). The ears were low set, prominent, and dysplastic. The nose was small, the lips were thin, and the mouth was large with downturning corners. The palate was highly arched and the chin was small. The initial cardiovascular examination was unremarkable. The extremities revealed moderate camptodactyly and clinodactyly of the fifth fingers, and metatarsus varus bilaterally. Dermatoglyphic examination showed four arches, three radial loops, two ulnar loops, and one whorl. There were deep palmar creases on the hands. The axial triradii and hallucal patterns were unremarkable. Cardiac catheterisation showed a large, membranous ventricular septal defect and a patent foramen ovale.
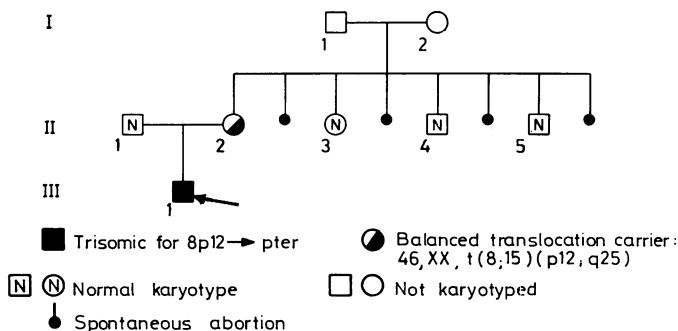

FIG 2 *Proband at age 3 months.*

FIG 1 *Pedigree of family.*

■ Trisomic for 8p12→ pter

◑ Balanced translocation carrier:
46,XX, t(8;15)(p12,q25)

N ⓝ Normal karyotype

□ ○ Not karyotyped

♦ Spontaneous abortion

The patient was readmitted at the age of 7 months with a history of cough, fever, and cyanosis. His weight (3520 g), height (55 cm), and head circumference (38·5 cm) were all below the 5th centile for his age. The new findings in the physical examination included periorbital and perioral cyanosis, hypotonia, decreased deep tendon reflexes, bilateral Babinski signs, and a grade 1/6 systolic ejection murmur at the left sternal border.

Radiological studies showed craniolacunia, an extra sacral segment, hypoplastic and bipartite ossification centres of the pubic bones, anomalous ribs with undulating and wavy contours and an excessive horizontal orientation, evidence of congenital heart disease with a large left to right shunt, retarded bone age, and brachymesophalangy of the second fingers.

He died during the surgical repair of the ventricular and atrial defects when he was 8 months old. The necropsy examination showed pulmonary effects of chronically raised pulmonary artery pressure secondary to congenital septal defects. The corpus callosum was intact and there was no renal abnormality. Post mortem cardiovascular diagnosis was severe hypertensive pulmonary arteriolar disease (Heath-Edwards grade 5-6).

CYTOGENETIC STUDIES
Chromosome studies of the proband and available family members were performed on peripheral leucocyte cultures. Slides were examined after G banding using trypsin. In all metaphases of the proband, extra chromosomal material on the long arm of chromosome 15 was observed: 46,XY,15q+. The karyotype of the mother (II.2) showed a balanced translocation between the short arm of chromosome 8 and the long arm of chromosome 15: 46,XX,t(8;15) (8qter→8p12::15q25→15qter; 15pter→15q25::8p12→8pter) (fig 3). Therefore,

the proband was trisomic for most of the short arm of chromosome 8(p12→pter) (fig 4). We assume that he must also be heterozygous for a small deletion of 15q(15q25→15qter). His karyotype can be formulated as: 46,XY,t(8;15)(p12;q25)mat according to Paris nomenclature. Karyotypes of the father, a maternal aunt, and two maternal uncles were normal. The maternal grandparents were not available for study.
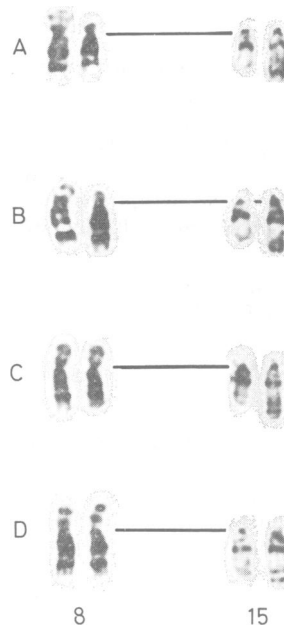

FIG 4   *G-trypsin banded chromosome 8 and 15 from two cells of the mother (A,B) and two cells of the proband (C,D).*
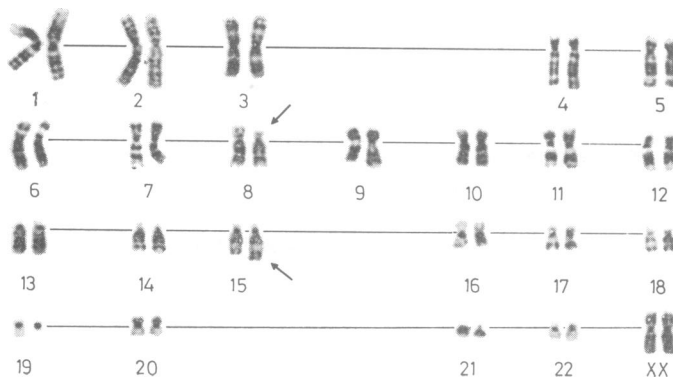

FIG 3   *G-trypsin banded karyotype of the mother: 46,XX,t(8;15)(p12;q25).*

Discussion

The karyotype-phenotype correlation in patients with trisomy 8 has been controversial. Riccardi[4] proposed the assignment of the clinical features of trisomy 8 to the q2 segment of chromosome 8. However, Rethoré et al[5] and Schinzel[6] argued from features found in patients with partial trisomies that extra material from both the long and short arms of chromosome 8 contributed to the clinical features of the trisomy 8 syndrome.

The present patient with only the short arm trisomy had most of the craniofacial features of trisomy 8 syndrome, including microcephaly, asymmetrical skull, hypertelorism, prominent nasal bridge, high arched palate, micrognathia, and low set, malformed ears. Although most of the patients with 8p trisomy did not have the major skeletal features of the trisomy 8 syndrome, the present patient had the cranial, vertebral, and rib anomalies. These findings provide further support for the view of Rethoré et al[5] and Schinzel[6] that extra chromosome material from both the short and the long arm segments of chromosome 8 are responsible for the clinical features of trisomy 8 syndrome.

Although clinical features of the 8p trisomy syndrome were thought to be non-specific,[3] the presence of deep skin creases, 'plis capitonnes', on the palms or soles can provide an important clue for the clinical diagnosis, as it did in the present patient.

Nearly all reported trisomy 8 patients have been mosaic, presumably because full trisomy in most instances would disturb embryogenesis sufficiently to cause intrauterine loss. The reported trisomy 8 mosaics generally have mild mental retardation and normal growth. However, the growth retardation and the clinical features in two cases of 8p trisomy, including the present patient and another patient reported by Clark et al,[7] were much more severe than those of trisomy 8 patients. This can be explained in part by the presence of extra chromosome material in each cell in the 8p trisomy group as opposed to mosaicism in the trisomy 8 patients. The associated monosomy in the formation of translocations, and the position effect on the expression of genes involved in the translocation, provide further explanation of the clinical severity in some cases of 8p trisomy.

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Aarskog's syndrome with Hirschsprung's disease, midgut malrotation, and dental anomalies

SUMMARY A 23-year-old man with Aarskog's syndrome had Hirschsprung's disease, midgut malrotation, a renal cyst, a cartilaginous projection of the pinna, geographic tongue, and dental anomalies. The family history, negative for these features, included several malignancies. Any or all of these features could be considered part of Aarskog's syndrome and may represent anomalies of neural crest development.